UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,031	06/20/2006	Yuntao Wu	GMU-11-004U	8029

28598 7590 12/15/2011

GEORGE MASON UNIVERSITY
OFFICE OF TECHNOLOGY TRANSFER, MSN 5G5
4400 UNIVERSITY DRIVE
FAIRFAX, VA 22030

EXAMINER	
KINSEY WHITE, NICOLE ERIN	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
12/15/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,031	WU ET AL.	
	Examiner	Art Unit	
	NICOLE KINSEY WHITE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-5,7-11,13-18,22,24,31,35 and 48* is/are pending in the application.

5a) Of the above claim(s) *48* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-5,7-11,13-18,22,24,31 and 35* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☒ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

The disclosure remains objected to because of the following informalities: The specification contains blanks at pages 5, 6, 14, 15 and 16. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 35 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that a specific host cell is required to practice the claimed invention. As such, the host cell must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the host cell.

The host cells disclosed in the specification do not appear to be produced from a repeatable process, and it is not apparent if the host cells are both known and readily

available to the public. It is noted that pages 6, 14, 15 and 16 of the specification indicate that the host cells have been deposited with the ATCC and applicants have submitted a Data Sheet indicating the deposit of the cells at the NIH AIDS Research & Reference Reagent Program. However, there is no indication in the specification as to deposit numbers for the NIH AIDS Research & Reference Reagent Program or the ATCC or to the public availability of the deposits.

If the deposit was made under the terms of the Budapest Treaty, then a statement, affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, or someone empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

If the deposit was not made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CRF 1.801-1.809 and MPEP 2402-2411.05, applicants may provide assurance of compliance by statement, affidavit or declaration or by someone empowered to make the same or by a statement by an attorney of record over his or her signature and registration number showing that:

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Response to Applicant's Arguments

Applicant has argued that the cells have been deposited at the NIH AIDS Research & Reference Reagent Program and thus, are publicly available.

In order for a biological sample to be considered known and readily available to the public there can be no restrictions placed on the availability of the material. At page 2 of the Data Sheet for Reagent No. 11467 under the heading "NOTE," the document raises concerns that the material may not be available if used for commercial use. Therefore, it does not appear that the deposited material is readily available to the public.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-11, 13-18, 22, 24 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naldini et al. (Science, 1996, 272:263-267) in view of Olsen et al. (Journal of Acquired Immune Deficiency Syndromes, 1991, 4:558-567).

The claims are directed to an isolated nucleic acid molecule comprising:

a) a promoter, wherein the activity of the promoter is dependent on the presence of the human immunodeficiency virus (HIV) Tat protein;

b) at least one splice donor site and at least one splice acceptor site;

c) an expressible sequence which is not a wild-type HIV sequence, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site;

d) a Rev Responsive Element (RRE) from the human immunodeficiency virus; and

e) a psi (φ) site,

wherein elements (a)-(d) are operably linked; and wherein the at least one splice acceptor site is contained within the RRE; or a complement thereof.

Naldini et al. discloses a transfer vector comprising an HIV LTR, wherein the activity of the promoter is dependent on the presence of the human immunodeficiency virus (HIV) Tat protein; at least one splice donor site and at least one splice acceptor site; an expressible sequence which is not a wild-type HIV sequence (CMV-Lucif or CMV-LacZ); a Rev Responsive Element (RRE) from the human immunodeficiency virus; and a psi. The elements are operably linked.

Naldini et al. does not teach the limitations " wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site" and "wherein the at least one splice acceptor site is contained within the RRE."

However, it would have been obvious for and well within the purview of one of ordinary skill in the art to place the expressible sequence at any location within the construct of Naldini et al. The expressible gene has its own promoter (CMV) and does not depend on the other elements in the construct for expression. Naldini et al. states that the vector design allows the efficient transcription and cytoplasmic export of full-length vector transcripts only in the presence of HIV Tat and Rev. This efficient

transcription and cytoplasmic export will still occur regardless of the location of the expressible gene. Thus, Naldini et al. is able to detect HIV infection using the construct.

It would also be obvious for and well within the purview of one of ordinary skill in the art to place the splice acceptor (and donor) sites at any location within the construct, including in the RRE, such that the components of the construct functioned properly and such that splicing occurred in the absence of Rev. One of ordinary skill in the art would know not to place the splice sites in a location that would render the construct non-functional. In that regard, the regions critical for RRE function are known in the art. See, for example, Olsen et al. (Journal of Acquired Immune Deficiency Syndromes, 1991, 4:558-567), which discloses a stem loop structure with the RRE that is critical for Rev binding. Critical regions for the other components in the construct of Naldini et al., such as the promoter and Tat, are also known in the art. Thus, one of ordinary skill in the art would know where not to place the splice sites within the RRE or any other component. And, given the teachings of the prior art, one of ordinary skill in the art would reasonably expect that placement of a sequence within the non-critical regions of the RRE (or other component) would not disrupt RRE or splice acceptor function.

The choice and placement of splice donors and acceptors within a construct is well within the purview of one of ordinary skill in the art. Therefore, it would have been obvious to one of ordinary skill in the art to select HIV splice donors and acceptors (D1/A7 and/or D4/A5) or any other known splice donor and acceptor to incorporate into the claimed construct (in appropriate locations) and the results would have been

predictable. Choosing a particular splice donor and acceptor to include in a construct is routine.

The construct of Naldini et al. comprises the same components as the claimed construct, albeit in a slightly different order. Further, both constructs can be used to detect HIV infection (e.g., no splicing occurs when HIV Rev is present). Applicant has not shown that the order of the components of the claimed construct renders the claimed construct novel and patentable. Absent unexpected results, the claimed construct is obvious over the construct of Naldini et al.

As for claims 15, 17 and 18, it would be obvious for one of ordinary skill in the art to substitute a fluorescent protein as the reporter gene instead of luciferase or β-gal. Various fluorescent proteins such as green fluorescent protein are well known and routinely used as reporter genes. It is obvious to substitute one reporter gene for another and the results would be predictable. It is also obvious to substitute a therapeutic gene in the construct of Naldini et al. to treat HIV infected cells. Because the construct is designed to not splice in the presence of HIV Rev, the therapeutic gene transcript can be exported to the cytoplasm and translated into protein, thus treating the cell.

As for claims 10, 11 and 22, the components and organization of the components of these constructs are obvious as outlined above (e.g., GFP, splice donor and splice acceptor sites, and HIV LTRs are all known).

Claims 1-5, 7-11, 13-18, 22, 24 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mautino et al. (Human Gene Therapy, 2000, 11:895-908) in view of Olsen et al. (Journal of Acquired Immune Deficiency Syndromes, 1991, 4:558-567).

Mautino et al. discloses a transfer vector comprising an HIV LTR, wherein the activity of the promoter is dependent on the presence of the human immunodeficiency virus (HIV) Tat protein; at least one splice donor site and at least one splice acceptor site; an expressible sequence which is not a wild-type HIV sequence; a Rev Responsive Element (RRE) from the human immunodeficiency virus; and a psi. The elements are operably linked (see the constructs on page 898).

Mautino et al. does not teach the limitations " wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site" and "wherein the at least one splice acceptor site is contained within the RRE."

However, it would have been obvious for and well within the purview of one of ordinary skill in the art to place the expressible sequence at any location within the construct of Mautino et al. The expressible gene has its own promoter (e.g., CMV) and does not depend on the other elements in the construct for expression. In the presence of Rev, unspliced transcripts are exported to the cytoplasm. This cytoplasmic export will still occur regardless of the location of the expressible gene. Thus, Mautino et al. is able to detect HIV infection using the construct .

It would also be obvious for and well within the purview of one of ordinary skill in the art to place the splice acceptor (and donor) sites at any location within the construct, including in the RRE, such that the components of the construct functioned properly and such that splicing occurred in the absence of Rev. One of ordinary skill in the art would know not to place the splice sites in a location that would render the construct non-functional. In that regard, the regions critical for RRE function are known in the art. See, for example, Olsen et al. (Journal of Acquired Immune Deficiency Syndromes, 1991, 4:558-567), which discloses a stem loop structure with the RRE that is critical for Rev binding. Critical regions for the other components in the construct of Mautino et al., such as the promoter and Tat, are also known in the art. Thus, one of ordinary skill in the art would know where not to place the splice sites within the RRE or any other component. And, given the teachings of the prior art, one of ordinary skill in the art would reasonably expect that placement of a sequence within the non-critical regions of the RRE (or other component) would not disrupt RRE or splice acceptor function.

The choice and placement of splice donors and acceptors within a construct is well within the purview of one of ordinary skill in the art. Therefore, it would have been obvious to one of ordinary skill in the art to select HIV splice donors and acceptors (D1/A7 and/or D4/A5) or any other known splice donor and acceptor to incorporate into the claimed construct (in appropriate locations) and the results would have been predictable. Choosing a particular splice donor and acceptor to include in a construct is routine.

The construct of Mautino et al. comprises the same components as the claimed construct, albeit in a slightly different order. Further, both constructs can be used to detect HIV infection (e.g., no splicing occurs when HIV Rev is present). Applicant has not shown that the order of the components of the claimed construct renders the claimed construct novel and patentable. Absent unexpected results, the claimed construct is obvious over the construct of Mautino et al.

As for claims 14-18, it would be obvious for one of ordinary skill in the art to substitute other known reporter genes in place of the reported genes used by Mautino et al. Various reporter genes such as green fluorescent protein and luciferase are well known and routinely used as reporter genes. It is obvious to substitute one reporter gene for another and the results would be predictable. It is also obvious to substitute a therapeutic gene in the construct of Mautino et al. to treat HIV infected cells. Because the construct is designed to not splice in the presence of HIV Rev, the therapeutic gene transcript can be exported to the cytoplasm and translated into protein, thus treating the cell.

As for claims 10, 11 and 22, the components and organization of the components of these constructs are obvious as outlined above (e.g., GFP, splice donor and splice acceptor sites, and HIV LTRs are all known).

Response to Applicant's Arguments

In the reply dated October 20, 2011, applicant argues that the amendments to the claims overcome the obviousness rejections. Applicant's arguments have been fully considered but not found persuasive.

Applicant has amended the claims to state that the Rev Responsive Element (RRE) is located 3' to the promoter. It is not clear how this changes the claim as the RRE was originally 3' to the promoter (i.e., the 5' LTR).

The constructs of Naldini et al. and Mautino et al. have the RRE 3' to (i.e., to the right of) the LTR promoter. Further, changing the location of the RRE within the construct does not render the construct patentable. As stated above, the constructs of Naldini et al. and Mautino et al. comprises the same components as the claimed construct, albeit in a slightly different order. Both constructs can be used to detect HIV infection (e.g., no splicing occurs when HIV Rev is present). Applicant has not shown that the order of the components of the claimed construct renders the claimed construct novel and patentable over the constructs of the cited references. Absent unexpected results, the claimed construct is obvious over the constructs of Naldini et al. and Mautino et al.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on (571) 272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Nicole Kinsey White/
Examiner, Art Unit 1648

/Stacy B. Chen/
Primary Examiner, Art Unit 1648